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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,323	12/19/2005	David Gershon	JG-RP-5170PCT/US/500561.2	5879

26418 7590 09/23/2008

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EXAMINER	
ZAREK, PAUL E	

ART UNIT	PAPER NUMBER
4161	

MAIL DATE	DELIVERY MODE
09/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,323	GERSHON, DAVID	
	Examiner	Art Unit	
	PAUL ZAREK	4161	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/19/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-14 are currently pending. This is the first Office Action on the merits of the claim(s).

Priority

2. The priority paragraph in the preliminary amendment claims priority to PCT/JP2004/19812, which is the wrong international application. The priority paragraph added in the preliminary amendment should be amended to indicate that the instant application is the national stage filing of under 35 U.S.C. 371 of PCT/US04/19812, which was filed on June 21, 2004, and which claims priority to U.S. Provisional Application 60/480,206, filed June 20, 2003.

Specification

3. The disclosure is objected to because of the following informalities:

- There are numerous superscript numbers throughout the text. It is unclear to what these superscript numbers refer.
- Table 9 (pg 14) does not disclose the definitions of the two right most columns. It is unclear what the different columns measure.

Appropriate correction is required.

Claim Objections

4. Claims 5 and 12 are objected to because of the following informalities: The claims limit the animal to be treated to, among others, a dog sheep. Examiner interprets the intent of the Applicant to treat a dog and/or a sheep. Insertion of a comma between dog and sheep is suggested. Appropriate correction is required.

5. Claims 6 and 13 are objected to because of the following informalities: The claims are drawn to treating or preventing "nongenital skin arts," among others. Examiner interprets the intent of the Applicant to treat nongenital skin warts. Appropriate correction is required.

6. Claims 7 and 14 are objected to because of the following informalities: The claims contain two periods floating in the claim and lack a period at the end. The floating periods are located the in following: ". . . Cervical Cancer,. Nonmalignant . . ." and "oral verruca vulgaris, .and Focal . . .." Appropriate correction is required.

Claim Rejections - 35 USC § 112 (1st paragraph)

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

9. *In re Wands*, 858 F.2d at 736-40, 8 USPQ2d at 1403-07, set forth eight factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (MPEP § 2164.01(a))

a. *The breadth of the claim*: Claims 1-7 are drawn to a method of treating a disease caused by papilloma virus in a subject comprising administration of CTC-96. Claims 8-14 are drawn to a method of inhibiting or preventing a disease caused by papilloma virus. Claims 2-5 and 9-12 limit the subject to be treated. Claims 6, 7, 13, and 14 limit the disease to be treated;

b. *Nature of the invention*: The nature of the invention is adequately described in section a;

c. *The state of the prior art*: The prior art is unequivocal when it states that while CTC-96 is effective against some viruses, it "is not a global virus inhibitor since it is ineffective in the cottontail rabbit papillomavirus model." (Schwartz, et al., Journal of Virology, 2001, pg 4117, col 2, lines 15-17, emphasis added). Ostrow, et al., (Antiviral Research, 1994) was under contract with NIAID to screen, *in vivo*, putative anti-papillomavirus agents (pg 28, lines 3-5). In their screen of CTC-96, which they received from Redox Pharmaceuticals, the assignee of the instant application, Ostrow, et al., found that rabbits treated with CTC-96 displayed a dose-dependent increase in tumor size, time to first tumor, and number of rabbits developing tumor (Table 1). The differences were statistically significant with $P<0.001$ for tumor size. Ostrow, et al., state that their results,

"show that the use of [CTC-96] may be contraindicated in patients with papillomavirus" (pg 29, lines 9-10, emphasis added) ;

d. *Level of one of ordinary skill in the art*: Clinicians and scientists investigating antiviral therapy, and specifically anti-papillomavirus therapy would constitute one of ordinary skill in the art;

e. *Level of predictability in the art*: The art suggests that there is no unpredictability with regards to treatment of papilloma virus with CTC-96. The drug is not effective;

f. *Amount of direction provided by the inventor*: Applicant suggests that CTC-96 can be an effective treatment for papilloma virus infection, or prevent said infection. Applicant discloses that CTC-96 forms stable adducts with the imidazole nitrogens of histidines in proteins to affect viral penetration and cell-to-cell spreading. CTC-96 appears to be effective against HSV and HIV mutants resistant to currently used drugs. Applicant discloses the mechanism by which CTC-96 operates. Applicant also supplies *in vitro* and *in vivo* working examples (discussed below);

g. *Existence of working examples*: Applicant provides both *in vitro* and *in vivo* examples. The results disclosed in Tables 1-8 disclose the effects of CTC-96 treatment on tumor growth, graft histology, and the presence of HPV-11 in grafts. Applicant claims that CTC-96 effects a "small but significant effect on the infectivity of HPV-11," but provides no values of significance (i.e. a P value). The standard deviation of the control group (no CTC-96 in the topical cream) is notably large (±0.808) (Table 1). Table 5 also discloses graft size in animals and shows that the administration of CTC-96 promotes enhanced tumor growth relative to control (91.39 v. 57.5, respectively). The

standard deviation is notably large for all groups tested, and no values of significance are provided. Applicant notes "[t]he ANOVA fails to show a treatment effect on the growth of individual grafts" (instant specification, pg 10, paragraph 00032). Tables 2-4 and 6-8 demonstrate that CTC-96 reduces the presence of HPV-11 in histology, immunocytochemistry, and RT-PCR experiments from explanted grafts. Applicant provides no working examples of CTC-96 preventing HPV infection, *in vivo*.

The results disclosed in Tables 9-11 demonstrate that treatment of C127 mouse epithelial cells, *in vitro*, with CTC-96 effectively inhibits bovine papilloma virus from transforming said cells; and,

h. *Quantity or experimentation needed to make or use the invention based on the content of the disclosure*: While the *in vitro* data is convincing, the claims of the instant application are not drawn to a method of preventing papilloma virus from infecting cells, or treating cells already infected with papilloma virus. The instant claims are drawn to methods of treating subjects suffering a disease caused by papilloma virus with a composition comprising CTC-96. Therefore, examples demonstrating the effectiveness of CTC-96, *in vitro*, are not given as much weight as *in vivo* data demonstrating that the drug would effectively treat diseases caused by papilloma virus. The *in vivo* working examples provided are not convincing, as any effect CTC-96 had on inhibiting tumor growth was minimal at best. Even though CTC-96 appeared to completely remove all traces of HPV-11 from the graft, the fact of the matter is that the grafted tumors continued to grow. The proof is in the pudding, so to speak, in that the presence of papilloma virus within the graft is irrelevant if the graft continues to grow. Applicant

even admits that there appeared to be no treatment effect on the growth of individual grafts (pg 10, paragraph 0032). The deficiencies of the instant specification are in no way compensated by the prior art. In fact, the prior art states that CTC-96 should not be used to treat papilloma virus infections as administration of CTC-96 promoted tumor growth and metastasis (Ostrow, et al., pg 29, lines 9-10). In order to make and use the invention commensurate in scope with the instant specification, one skilled in the art at would have to completely ignore the prior art stating that CTC-96 is not an effective treatment for papilloma virus infection, and provide their own guidance because the instant specification does not demonstrate that CTC-96 effectively treats papilloma virus infection, as evidenced by the fact that tumors grew regardless of whether the mice were treated with CTC-96. Therefore, the instant specification does not enable one of ordinary skill in the art to use the invention commensurate with the scope of the rejected claims.

Claim Rejections - 35 USC § 112 (2nd paragraph)

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejected claims are drawn to a method comprising administration of "an anti-papilloma virus disease effective amount of CTC-96." It is unclear what the metes and bounds of this limitation are, therefore the claim is indefinite.

Conclusion

12. No claims are allowed

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL ZAREK whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, PATRICK NOLAN can be reached on (571) 272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/Ashwin Mehta/
Primary Examiner, Technology Center 1600